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OPTIMAL SINGULAR CONTROLS FOR VSEIR MODEL OF TUBERCULOSIS

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***Abstract*—The optimality singular controls of a VSEIR model of Tuberculosis are analyzed in this paper. There are controls that correspond to time- vary the vaccination and treatment schedules. A Hamiltonian (H) of the model is defined. The model is splited into separate one-dimensional problems, the so-called switching functions. The extreme occurs when a switching function disappears suddenly over an open interval. In which the derivatives of switching function must disappears suddenly and this typically allows computing such a control. The second-order of the function is not vanishing, which satisfied Legendre-Clebsh condition, and thus the controls of these kinds are called singular. In this work, our main emphasis is on a complete analysis of the optimum properties corresponding to trajectories. The result shows that vaccination control is singular, but treatment is not. This means that the model reached the optimality control for vaccination schedule, but not treatment schedule.**

Keywords: VSEIR model; Singular control; Legendre-Clebsh; switch functional

I. INTRODUCTION

Tuberculosis (TB) acquired through airborne infection and, most commonly affects the lungs. TB is a bacterial disease caused by Mycobacterium Tuberculosis, which is transmitted through contaminated air that are released during coughing TB patients. TB disease can affect anyone and anywhere, and generally in children. The source of infection is derived from adult TB patients [1]. TB infection can infect virtually all body because the bacteria can spread through the blood vessels or lymph nodes. Although the organs most commonly affected are the lungs, but in people with a low immune system can infect the lungs, brain, kidneys, gastrointestinal tract, bone, lymph nodes, etc [1]. Molliq et al. [2] modified adopted Exposed class to Vaccination Susceptible Infected Recovery (VSIR) model which proposed by Momoh et al. [3]. Efforts to eliminate a disease that can be managed optimally spread will be reached by the stage of research, the application of new methods, the development of several diagnostic tools, drugs and new vaccines. Optimization of the control of the disease control needs a study of optimization model[4]. Optimization of dynamical systems in general use optimal control, where the solving problem of optimal control using the famous and wide used approach i.e. Pontryagin maximum principle with Legendre-Clebsch condition [5-6].

In this paper, we analysed the optimal singular control of VSEIR model [2]. Here, any interaction between exposed and infected is investigated using a Legendre-Clebsch condition. Ledzewicz and Schatter [7] analyzed the optimal singular controls of a general SIR model with vaccination and treatment. It showed that control for vaccination was singular, but not treatment. Based on [7], we will show the optimal singular control of VSEIR model to see the schedule of controlling on vaccination and infected variable.

II. FORMULATION OF EPIDEMIOLOGICAL MODEL

We only consider the epidemiology model of type VSEIR [2] which has five classes. The class V represents vaccination, S represents the susceptible who do not have the disease, E represents the exposed who are infected but are yet to show any sign of symptoms, I represents the infective who have the disease and can transmit it to others, R denotes the recovered population who went through infection and appear with permanent or temporary infection which need immune. the total number of individuals was denoted S by $N(t)$ which divided into four distinct epidemiological subclasses of individuals. Let $V(t), S(t), I(t)$, and $R(t)$, represent the vaccination, susceptible, infectious, and recovered, respectively. Thus, $N(t)$ can be written as $N(t) = V(t) + S(t) + I(t) + R(t)$. The VSIR model [4] having vaccination, infected and recovered period is described by the following dynamic system:

$$\dot{V} = qN - \delta_1 V S - \mu_1 V, \quad (1)$$

$$\dot{S} = \delta_1 V S - \mu_2 S - \alpha E S, \quad (2)$$

$$\dot{E} = \alpha E S - \mu_3 E - \rho E I, \quad (3)$$

$$\dot{I} = \rho E I - \beta I, \quad (4)$$

$$\dot{R} = \delta_4 I - \gamma R, \quad (5)$$

The controlled mathematical model when $\beta = \mu_4 +$

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$\mu_{TB} + \delta_4$, where human birth in natural through passive vaccination $(V\ (t))$ at rate q, nonnegative parameters μ_1, μ_2, μ_3 and μ_4 denote as natural death of population of the V, the S, the E the I and the R, respectively. Population of infected Tuberculosis died in rate μ_{TB}. The susceptible population decreased due to coming individual from the V in rate δ_1 denotes the transfer rate from susceptible to infected population. Influence of Exposed to infect is increased in rate ρ. Infected population increases due to movement of individuals from infected individuals I in rate δ_4 and it decreased due to movement of individuals in to the S at rate α. In this paper, we assume that human is fully recovered and R population will be decreased due to movement of individuals to the R at rate γ. In the flow of mathematical model, we assume that each compartment occurs interaction between classes.

Thus there are two possible mechanisms as controls: immunization of the vaccination, susceptible and exposed individuals and treatment of the infected ones. These models controlled by the two controls u and v that are taken as Lebesque-measurable functions. The controls improves the class R of the recovered individuals by removing them from the class of vaccination, susceptible and infected ones, respectively. The class R is defined as $R = N - V - S - E - I$. To ensure the model to be reliable, make sure that all the variables which included R *remain* positive. The initial value of VSEIR model denoted by

$$N(0) = N_0, V(0) = V_0, S(0) = S_0, E(0) = E_0, \quad \text{and} \quad I(0) = I_0. \tag{6}$$

From biological considerations, a closed set

$$Q = \{(V,S,E,I) \in \mathbb{R}^4 : V,S,E,I > 0, \; V+S+E+I < N\}, \tag{7}$$

where $\mathbb{R}^4$ denotes the non-negative cone and its lower dimensional faces. It can be verified that Q is positively invariant with respect to Eqs. (1)-(5). We denote by ∂Q and $\dot{Q}$ the boundary and the interior of Q.

III. OPTIMAL CONTROL PROBLEM FORMULATION

Our objective is, to investigate the best strategy in terms of vaccination and treatment that will minimize the number of people who die because of the infection while at the same time minimizing the cost of the vaccination and treatment of the population. Let the population sizes of all five classes, V_0, S_0, E_0, I_0 and R_0 are given. We consider the following objective for a fixed terminal time T:

$$J(u,v) = \int_0^T (a_1 V + a_2 S + (a_3 + c_3)u + a_4 v)dt. \tag{8}$$

where $a_1\, V\,(t)$ denotes the number of vaccination at time t, $a_2\, I\,(t)$, represents the individuals who are exposed and infected at time t and are symbol a_2 is measure of the deaths associated with the outbreak. The terms, $(a_3 + c_3)u(t)$ and $a_4\, v(t)$ defines the cost of vaccination and treatment, respectively. Here, $(a_3 + c_3)$ and a_4 are assumed to be proportional to the vaccination and treatment rates. We apply a methods of geometric optimal control theory to analyse the relations between optimal vaccination and treatment schedules. These techniques become more clear if the problem is formulated as a Mayer-type optimal control problem: that is, one where we only minimize a penalty term at the terminal point. Such a structure can easily be achieved at the cost of one more dimension if the objective is adjoined as an extra variable. Defining

$$\dot{Z} = a_1 V + a_2 S + (a_3 + c_3)u + a_4 v, \quad \text{and} \quad Z(0) = Z_0 \tag{9}$$

We therefore consider the following optimal control problem. For a fixed terminal time, minimize the value $Z\,(T)$ subject to the dynamics

$$\dot{Z} = a_1 V + a_2 S + (a_3 + c_3)u + a_4 v, \quad \text{and} \quad Z(0) = Z_0, \tag{10}$$

$$\dot{V} = qN - \delta_1 V S - \mu_1 V - uV, \text{ and } V(0) = V_0, \tag{11}$$

$$\dot{S} = \delta_1 V S - \mu_2 S - \alpha ES - uS, \quad \text{and} \quad S(0) = S_0, \tag{12}$$

$$\dot{E} = \alpha ES - \mu_3 E - \rho EI - uE, \text{ and } E(0) = E_0, \tag{13}$$

$$\dot{I} = \rho EI - \beta I - vI, \text{ and } I(0) = I_0, \tag{14}$$

where $\beta = \mu_4 + \mu_{TB} + \delta_4$. For all Lebesque measurable functions $u : [0,T] \to [0, u_{max}]$ and $v : [0,T] \to [0, v_{max}]$,

We introduce the state $x' = (Z,V,S,E,I)^T$, the dynamics of system is multi input control affine system of the form

$$\dot{x} = f(x) + g_1(x)u + g_2(x)v \tag{15}$$

with drift vector field f given by

$$f(x) = \begin{pmatrix} a_1 V + a_2 I \\ qN - \delta_1 VS - \mu_1 V \\ \delta_1 VS - \mu_2 S - \alpha ES \\ \alpha ES - \mu_3 E - \rho EI \\ \rho EI - \beta I \end{pmatrix} \tag{16}$$

and control vector fields g_1 and g_2 are written as

$$g_1 = \begin{pmatrix} a_3 + c_3 \\ -V \\ -S \\ -E \\ 0 \end{pmatrix} \text{ and } g_2 = \begin{pmatrix} a_4 \\ 0 \\ 0 \\ 0 \\ -I \end{pmatrix}.$$

A controlled trajectory of the system is defined admissible control pair (u,v) with corresponding solution x.

IV. NECESSARY CONDITIONS FOR OPTIMALITY

Let a row-vector $\lambda = (\lambda_1, \lambda_2, \lambda_3, \lambda_4) \in \mathbb{R}^4$ from first-order necessary conditions for optimality of a controlled trajectory by the Pontryagin maximum principle [7-8]. Then, the Hamiltonian $H = H(\lambda, x, u, v)$ are defined as the dot product, $<,.,.>$ of the row vector λ with the column vector defining the dynamics, that is

$$H = \langle \lambda, f(x) + g_1(x)u + g_2(x)v \rangle,$$

$$= \lambda_1(a_1V + a_2S + (a_3 + c_3)u + a_4v) + \lambda_2(qN - \delta_1 VS - \mu_1 V - uV) + \lambda_3(\delta_1 VS - \mu_2 S - \alpha ES - uS) + \lambda_4(\alpha ES - \mu_3E - \rho EI - uE) + \lambda_5(\rho EI - \beta I - vI). \quad (17)$$

Afterward, if (u_*, v_*) is optimal control defined over interval $[0, T]$ with corresponding trajectory $x_* = (Z_*, V_*, S_*, E_*, I_*)^T$ there is exist an absolutely continuous co-vector $\lambda: [0, T] \to (\mathbb{R}^4)^*$, so that following conditions hold [8]

(a) λ satisfies the adjoin equation (written as row vector and with D_f and D_{g_i}denote the Jacobian matrices of the partial derivatives)

$$\dot{\lambda} = -\lambda(Df(x_*) + Dg_1(x_*)u_* + Dg_2(x_*)v_*), \quad (18)$$

with terminal condition

$$\lambda(T) = \left(\frac{q}{\mu_1}, 0,0,0\right), \quad (19)$$

(b) For every time $t \in [0, T]$, the optimal controls $(u_*(t), v_*(t))$ minimize the Hamiltonian along $(\lambda(t), x_*(t))$ over the control set $[0, u_{max}] \times [0, v_{max}]$, and

(c) Hamiltonian is constant along the optimal solution.

A pair $(x, (u, v))$ consisting of controls (u, v) with corresponding trajectory x for which there are exist multipliers λ so that the conditions of the Maximum Principle are satisfied an external (pair) and the triple $(x, (u, v), \lambda)$ is an external lift. Note that the dynamics does not depend on the auxiliary variable Z and thus by the adjoin equation (6) the multiplier λ_1 is constant; by the terminal condition (20), thus, it is given by $\lambda_1(t) = \frac{q}{\mu_1}$. Particularly, the overall multiplier $\lambda(t)$ cannot be zero. For almost any time t, the optimal controls $(u_*(t), v_*(t))$ minimize the Hamiltonian $H(\lambda(t), x_*(t), u, v)$ over the compact interval $[0; u_{max}] \times [0; v_{max}]$. Afterward, defining the so-called switching functions Φ_1 and Φ_2 as

$$\Phi_1 = \langle \lambda(t), g_1(x_*(t)) \rangle = (a_3 + c_3) - \lambda_2(t)V_*(t) - \lambda_3(t)S_*(t) - \lambda_4(t)E_*(t) \quad (20)$$

And

$$\Phi_2 = \langle \lambda(t), g_2(x_*(t)) \rangle = a_4 - \lambda_5(t)I_*(t) \quad (21)$$

It follows that the optimal controls satisfy

$$u_*(t) = \begin{cases} 0 & if \quad \Phi_1(t) > 0, \\ u_{max} & if \quad \Phi_1(t) < 0, \end{cases}$$

and

$$v_*(t) = \begin{cases} 0 & if \quad \Phi_2(t) > 0, \\ v_{max} & if \quad \Phi_2(t) < 0, \end{cases}$$

The minimum condition alone does determine the controls at times when $\Phi_1(t) = 0$. If $\Phi_1(t) = 0$, but $\dot{\Phi}_1(t) \neq 0$, then the control switches between the value 0 and its maximum value depending on the sign of $(\dot{\Phi}_i)(t)$. The other extreme occurs when a switching function disappears suddenly over an open interval. In this case also derivatives of $\Phi_1(t)$ have to disappear and then allows to compute such a control. Controls of this kind are called singular [7]. Singular controls tend to be either that minimizing or the maximizing strategies and in either case they are essential in determining the structure of optimal controls. We have to synthesize from singular controls through an analysis of the switching function. Thus singular controls generally play a major role in a synthesis of optimal controlled trajectories. In this work, the existence of the problem and local problem in Eqs. (11)-(14) will be analysed. An vital implement in this analysis is the Lie bracket of vector fields which generally arises in the formulas for the derivatives of the switching function. Give two differentiable vector fields f and g defined on a common open subset of $\mathbb{R}^4$, their Lie bracket can be defined as

$$[f, g](x) = Dg(x)f(x) - Df(x)g(x). \quad (22)$$

The Lie-bracket is anti-commutative, i.e., $[f, g] = -[g, f]$, and for arbitrary vector fields f, g and h it satisfies the Jacobi identity [7]

$$[f, [g, h]] + [g, [h, f]] + [h, [f, g]] = 0. \quad (23)$$

The following result provides an elegant and important framework for efficient computations of the derivatives of the switching functions. It is easily done by computation.

Proposition IV.1. *Let $(x, (u, v))$ be a controlled trajectory of the system and let λ¸ be a solution to the corresponding adjoint equations. Given a continuously differentiable vector field h, define*

$$\psi(t) = \langle \lambda(t), h(x(t)) \rangle. \quad (24)$$

Then the first derivative of ψ is given by

$$\psi(t) = \langle \lambda(t), [f + g_1u + g_2v, h](x(t)) \rangle. \quad (25)$$

V. THE STRUCTURE OF SINGULAR CONTROLS

For the system in Eqs. (11)-(14), we will investigate the existence and local optimality of singular controls. By Propositions IV.1 the derivatives of the switching functions $\Phi_1(t) = \langle \lambda(t), g_1(x(t)) \rangle$ and $\Phi_2(t) = \langle \lambda(t), g_2(x(t)) \rangle$ are written as

$$\dot{\Phi}_1(t) = \langle \lambda(t), [f + g_1u + g_2v, g_1](x(t)) \rangle, \quad (26)$$

$$\dot{\Phi}_2(t) = \langle \lambda(t), [f + g_1u + g_2v, g_2](x(t)) \rangle. \quad (27)$$

By anti-commutative of the Lie bracket $[g_i, g_i] \equiv 0$ and a easily computation confirms that the control vector fields g_1 and g_2 commute, i.e., $[g_1, g_2] \equiv 0$ as well. We thus have that

$$\dot{\Phi}_1(t) = \langle \lambda(t), [f, g_1](x(t)) \rangle \quad (28)$$

and

$$\dot{\Phi}_2(t) = \langle \lambda(t), [f, g_2](x(t)) \rangle. \quad (29)$$

Elementary calculations verify that

$$[f, g_1](x) = \begin{pmatrix} a_1V \\ -\delta_1SV - qN \\ \delta_1SV - \alpha ES \\ \alpha ES \\ \rho IE \end{pmatrix} \quad (30)$$

and

$$[f,g_2](x)=\begin{pmatrix} a_3I \\ 0 \\ 0 \\ -\rho IE \\ 0 \end{pmatrix}. \quad (31)$$

First, we analyse the control, i.e., vaccinations schedules. Applying Propositions IV.1 again to $\dot{\Phi}_1$, it follows that

$$\ddot{\Phi}_1(t)=\langle\lambda(t),[f+g_1u+g_2v,[f,g_1]](x(t))\rangle. \quad (32)$$

A direct calculation shows that g_2 and $[f,g_1]$ commute as well $[g_2,[f,g_1]]=\begin{pmatrix}0\\0\\0\\0\\0\end{pmatrix}$, and that

$$[g_1,[f,g_1]]=\begin{pmatrix} -a_1V \\ -\delta_1SV-qN \\ \alpha SE-\delta_1SV \\ -\alpha ES \\ -\rho IE \end{pmatrix}. \quad (33)$$

The relation

$$\dot{\Phi}_1=\lambda_1(a_1V)-\lambda_2(\delta_1SV+qN)+\lambda_3(\delta_1SV-\alpha SE)+\lambda_4\alpha ES+\lambda_5\rho IE=0, \quad (34)$$

suppose

$$\lambda_4\alpha ES+\lambda_5\rho IE=\lambda_1(a_1V)-\lambda_2(\delta_1SV+qN)+\lambda_3(\delta_1SV-\alpha SE). \quad (35)$$

Implies that

$$\langle\lambda(t),[g_1,[f,g_1]](x(t))\rangle=-2\lambda_1(t)a_1V-2\lambda_2\delta_1SV \quad (36)$$

and $\Phi_1(t)=\lambda_1(t)(a_3+c_3)-\lambda_2(t)V-\lambda_3(t)E-\lambda_4(t)I\equiv 0$ gives that $\lambda_2(t),\lambda_3(t)$ and $\lambda_4(t)$ have to be positive along a singular arc. Hence we obtain

$$\langle\lambda(t),[g_1,[f,g_1]](x(t))\rangle=-2\lambda_1(t)a_1V-2\lambda_2\delta_1SV<0. \quad (37)$$

Singular controls of Eq. (37) for which $\langle\lambda(t),[g_1,[f,g_1]](x(t))\rangle$ does not disappear suddenly, are said to be of order 1 and it is a second-order necessary condition for minimality, the so-called Legendre-Clebsh condition, that this value is negative [8]. Thus for this model singular controls u are locally optimal. Furthermore, we taking into account that $[g_1,[f,g_1]]=\begin{pmatrix} -a_1V \\ -\delta_1SV-qN \\ \alpha SE-\delta_1SV \\ -\alpha ES \\ -\rho IE \end{pmatrix}$, we can compute the singular control as

$$\mu_{Sin}=\frac{\langle\lambda(t),[f,[f,g_1]](x(t))\rangle}{\langle\lambda(t),[g_1,[f,g_1]](x(t))\rangle}. \quad (38)$$

Here,

$$[f,[f,g_1]](x)=\begin{pmatrix} -a_2\rho EI+2a_1qN-a_1\mu_1V \\ -2\delta_1qNS+\mu_2\delta_1SV-\mu_1qN \\ \alpha\rho ESI+\alpha\mu_3SE+2q\delta_1NS-\mu_1\delta_1SV \\ \rho^2E^2I-\alpha\mu_2ES \\ -\rho^2I^2E-\mu_3\rho EI \end{pmatrix} \quad (39)$$

Then

$$\mu_{Sin}=\big(\lambda_1(-a_2\rho EI+2a_1qN-a_1\mu_1V)+\lambda_2(-2\delta_1qNS+\mu_2\delta_1SV-\mu_1qN)+\lambda_3(\alpha\rho ESI+\alpha\mu_3SE+2q\delta_1NS-\mu_1\delta_1SV)+\lambda_4(\rho^2E^2I-\alpha\mu_2ES)+\lambda_5(-\rho^2I^2E-\mu_3\rho EI)\big)/\big(\lambda_1(-a_1V)+\lambda_2(-\delta_1SV-qN)+\lambda_3(\alpha SE-\delta_1SV)-\lambda_4(\alpha ES)-\lambda_5(\rho IE)\big). \quad (40)$$

Thus, the result can be written as follow

Proposition V.1. *A singular control u which has order* 1 *and satisfies the Legendre-Clebsch condition for minimality [8]. The singular control is given as a function that respect to unkno, depends on the both state and the multiplier in the following form*

$$\mu_{Sin}=\big(\lambda_1(-a_2\rho EI+2a_1qN-a_1\mu_1V)+\lambda_2(-2\delta_1qNS+\mu_2\delta_1SV-\mu_1qN)+\lambda_3(\alpha\rho ESI+\alpha\mu_3SE+2q\delta_1NS-\mu_1\delta_1SV)+\lambda_4(\rho^2E^2I-\alpha\mu_2ES)+\lambda_5(-\rho^2I^2E-\mu_3\rho EI)\big)/\big(\lambda_1(-a_1V)+\lambda_2(-\delta_1SV-qN)+\lambda_3(\alpha SE-\delta_1SV)-\lambda_4(\alpha ES)-\lambda_5(\rho IE)\big). \quad (41)$$

Firstly, we define the switching function as

$$\Phi_2=\langle\lambda(t),g_2(x(t))\rangle=a_2\lambda_1I-\rho\lambda_4IE. \quad (42)$$

By using proposition IV.1, the first derivative of Eq. (34) we have

$$\dot{\Phi}_2=\langle\lambda(t),[f,g_2](x(t))\rangle=a_2\lambda_1I-\rho\lambda_4I. \quad (43)$$

As we know, to check the optimally of Eq (34), Eq. (35) will be zero, we obtain

$$\langle\lambda(t),[f,g_2](x(t))\rangle=a_2\lambda_1I-\rho\lambda_4I=0. \quad (44)$$

Hence, we have

$$\ddot{\Phi}_2=\langle\lambda,g_2,[f,g_2]\rangle=0 \quad (45)$$

for minimality, the Legendre-Clebsh condition, that this value is negative [7]. Then, the singular controls v of VSEIR model is not locally optimal. Thus, we obtain the following result:

Proposition V.2. *The singular control v is not optimal.*

VI. CONCLUSION

The optimal singular control problem for an VSEIR-model of Tuberculosis was discussed and a Hamiltonian H of model is defined. The structure of singular controls was analysed to determine singularity properties of the model. We apply Lie bracket of vector field to check whether the second order of switching function was disappeared or not and the model splits into separate one-dimensional problems. Based on our computation by using Maple, the result shows that vaccination control is singular, but treatment is not. We found that the vaccination schedule was singular, but treatment schedule was not singular. The optimality of vaccination and treatment for other epidemiology problem can be analysed in future.

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